

REMARKS

A. The claims fulfill the requirements of 35 U.S.C. §112, second paragraph

The Examiner asserts that the phraseology in the claims is ambiguous in that claims 1, 2 and 13 refer to "skin or another external body surface," taking the position that "[e]ssentially all external surfaces are covered by skin." To the contrary, Applicants respectfully contend that other types of external body surfaces, such as mucous membranes of the, *inter alia*, the mouth and other surfaces like the scalp and cornea of the eye would be understood to be susceptible to wounds and would fall within the scope of the instant claims.

Applicants have amended claims 1 and 13 to read "presence and absence" rather than "presence or absence" to remove any confusion in the way the claims read, and thank the Examiner for his clarifying remarks.

Claims 3-4, 6-7, 14-16, 18-19, 25-26, 28-31, 33-34, and new claim 35, all depend from claims 1 and 13. Thus, Applicants respectfully submit that none of the pending claims are indefinite in view of their amendments and remarks set forth herein. Applicants therefore respectfully request withdrawal of rejection on these grounds.

B. The claims fulfill the requirements of 35 U.S.C. §112, first paragraph

The Examiner has rejected claims 1-4, 6-7, 13-16, 18-19, 25-26, 28-31, and 33-34 for failing to provide enablement for identifying any compound that improves treatment of wounds to skin in a diabetic animal on the ground that the invention does not provide a necessary link between finding a particular compound or narrowing the range of candidates in order to find a suitable compound without the need for undue experimentation.

Although disagreeing with the Examiner's position, in an effort to expedite prosecution of the pending claims Applicants have amended independent claims 1 and 13 to limit the claimed methods to identifying aldose reductase inhibitors that improve wound healing. No undue experimentation is needed to practice the steps of the claimed methods. A wide variety of aldose reductase inhibitors are known to those skilled in the art (as illustrated, *inter alia*, by compounds disclosed in U.S. Patent Nos. 5,700,819, 4,868,301, 5,330,997, and 5,236,945).

Applicants assert therefore that the claimed methods are fully enabled by the Applicants' specification, and respectfully requests therefore that this rejection of all pending claims be withdrawn.

C. The claims are not obvious under 35 U.S.C. §103(a)

The Examiner has maintained the previously-asserted rejection of claims 1-4, 6-7, 13-16, 18-19, 25-26, 28-31, 33-34 under 35 U.S.C. §103(a) as being unpatentable over Chen et al., U.S. Patent 6,232,341 (Chen) in view of Jones et al., WO 99/50268 (Jones) and Spence, U.S. Patent 4,226,232 (Spence).

Applicants note that the disclosure of the Spence reference is cited "solely . . . to show the general knowledge in the art in comparatively assessing agents of choice in treating skin wounds." Applicants understand this characterization to admit that the teachings of the Spence reference bear no specific relevance to the claimed invention.

Applicants respectfully contend that the instant obviousness rejection is not properly supported by a combination of references providing the required teachings, suggestions or motivation to combine the references to achieve the claimed invention. Specifically, Applicants contend that the combination of references is deficient because 1) the Chen reference does not teach the practice of the technology disclosed therein on a diabetic animal; and 2) the teachings of the Jones reference are limited to treating diabetic neuropathy in sciatic nerve. Diabetic neuropathy is a pathological condition of the nerves in a diabetic. Specifically, the Jones reference teaches that aldose reductase inhibitors can be used to treat diabetic neuropathy in the sciatic nerve of a diabetic, due to the ability of such ARIs to reduce sorbitol accumulation in the nerve. (The Spence reference is admitted in the Office Action to add nothing to the disclosure of the two primary references.) The Jones reference is devoid of any teachings regarding wound healing, and neither teaches nor suggests any relationship between neuropathy and wound healing in diabetic animals.

One skilled in the art would not have been motivated to combine or modify the cited references, or have a reasonable expectation of success of achieving the claimed invention if the references were so combined, because the prior art was silent on the existence of any relationship between wound healing and neuropathy in diabetic animals. The Jones reference, the only reference that teaches ARIs, discloses the effects of the disclosed ARIs

on diabetic cataracts, retinopathy and neuropathy, and is directed to treating and/or preventing neuropathy. Jones is significantly silent on any effect whatsoever of ARIs on diabetic wound healing, and of the use of the wound healing model as an effective marker for neuropathy and neurological conditions associated with diabetes (cf. Applicants' specification at p. 8, lines 2-7). The effects of ARI on diabetic wound healing, and hence the use of ARI as positive control in assessing the effect of other therapeutic agents on diabetic wound healing is not taught or suggested in any cited references, taken alone or in combination.

Applicants respectfully contend that there is no evidence of record that one of ordinary skill in the art would combine the teachings of the Jones reference, limited to systemic administration of a compound to have an effect in a nerve located internally in an animal, with a reference (Chen) relating to testing compounds for treating wounds in a non-diabetic animal. If one of ordinary skill knew that ARIs are effective in increasing wound healing in a diabetic animal, then perhaps a *prima facie* obviousness rejection could be maintained. The Patent Office has not entered into evidence any prior art recognizing that ARIs have such desirable properties. Indeed, it is only Applicants' specification that provides such teachings, which of course cannot properly be used against the Applicant to support the instant obviousness rejection

Pursuant to the provisions of 37 C.F.R. §1.104(d)(2), Applicants respectfully request the Patent and Trademark Office to provide them in the next Office Action with any prior art reference teaching that an ARI would be expected to have wound-healing or wound healing promoting properties in a diabetic animal.

Moreover, the pending claims are not directed to wound healing in general, but wound healing in a diabetic animal. It was well known in the art at the time of the invention was made that diabetic wounds are significantly different from non-diabetic wounds. For example, diabetic wounds heal more slowly, have decreased innervation in the epidermis, and can often result in significant morbidity (see Applicants' specification at page 1, line 20 to page 2, line 22). Accordingly, one of skill in the art would recognize these unique properties and characteristics of diabetic wounds, and would recognize that generic disclosure related to wound healing in the prior art would not be sufficient to raise a *prima facie* obviousness determination against Applicants' claims directed specifically to wound healing in a diabetic animal.

Applicants respectfully contend that the cited art, taken alone or in combination, contains no teaching, suggestion or motivation to use compounds (ARIs) known and used for internal purposes (treatment of diabetic sciatic nerve neuropathy) to improve wound healing in a diabetic animal. Applicants further respectfully contend that this cited prior art, properly limited to what it does and does not teach, does not support rejection of any of the rejected claims under 35 U.S.C. §103(a).

Based on the foregoing, Applicants respectfully contend that the asserted obviousness rejection has been traversed by their argument and respectfully request that the Examiner withdraw these grounds of rejection.

CONCLUSIONS

It is believed that all requirements of patentability are fully met, and allowance of the claims is respectfully requested.

If the Examiner believes it to be helpful, the Examiner is invited to contact the undersigned attorney by telephone at (312) 913-0001.

Respectfully submitted,

McDonnell Boehnen Hulbert & Berghoff

By:

Kevin E. Noonan, Ph.D.
Registration No. 35,303

Date: April 27, 2004